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### REMARKS

The present application was filed with a total of 25 Claims. In the present Restriction Requirement, the Examiner has restricted the Claims into four Groups, with Claims 1-10 in Group I, drawn to a Gram-positive microorganism maintaining a mutation or deletion within a nucleic acid sequence that encodes an inactivated metalloprotease; Claims 11-20 in Group II, drawn to a formulated composition comprising an active metalloprotease; Claims 21-24 in Group III, drawn to an expression vector that comprises a nucleic acid sequence encoding an active metalloprotease, as well as a host cell transformed with the expression vector; and Claim 25 in Group IV, drawn to a method of use of a nucleic acid probe having a sequence complementary in whole or in part to a nucleic acid sequence encoding a metalloprotease gene, in detecting and isolating a metalloprotease gene in the genome of a Gram-positive microorganism. Applicant hereby confirms the election of Group I with traverse, and has cancelled Claims 11-25.

Applicant notes that the indication of the priority claim in the Specification has been added in the present amendments. As the priority claim was clearly indicated in the transmittal of the present application when filed, and a copy of the priority application was provided, Applicant respectfully submits that the priority claim was made at the time of filing and that the requirements have been met. Should the Examiner believe that a petition is necessary, Applicant will provide such a petition.

Applicant also notes that the Examiner has indicated that the Information Disclosure Statement (IDS) filed August 29, 2003 does not fully comply with the requirements of 37 C.F.R. §1.98, because four of the cited documents are entire books and no particular pages nor chapters are cited therein. Applicant respectfully submits that these references were cited solely to show the overall state of the art. Thus, no specific citations have been provided. Applicant appreciates the Examiner's efforts in identifying the Lazarevic *et al.* reference.

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Applicant notes that the Examiner has objected to the use of "MP" in Claims 1, 4 and 5, and the Claims 8 and 10 require grammatical correction. Applicant has provided the necessary amendments in the present Response. Applicants note that the Examiner has indicated that Claims 4 and 5 are free of the prior art, although they are subject to the rejections under 35 U.S.C. §§101 and 112, second paragraph, as discussed in greater detail below.

The Examiners rejections are addressed below in the following order:

- 1) Claims 1-5 stand rejected under 35 U.S.C. §101, as allegedly being directed to non-statutory subject matter;
- 2) Claims 1-3 and 5-10 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not meeting the written description requirement;
- 3) Claims 1-3 and 5-10 stand rejected under 35 U.S.C. §112, first paragraph as allegedly not meeting the enablement requirement;
- 4) Claims 1-10 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite;
- 5) Claims 1-3 and 6-10 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Ferrari *et al.* (U.S. Patent No. 5,264,366), or Sloma *et al.* (U.S. Patent Nos. 5,589,383 or 5,620,880); and
- 6) Claims 1-3 and 7 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Donovan *et al.* (U.S. Patent No. 5,759,538).

**1) The Claims Recite Patentable Subject Matter**

The Examiner has rejected Claims 1-5 under 35 U.S.C. §101, as allegedly being directed to non-statutory subject matter. Applicant must respectfully disagree. The Examiner argues that Claims 1-5 describe a *B. subtilis* cell that is a product of Nature because no claim states a descriptive recitation that the microorganism is the product of an activity of a person. In order to more clearly describe the claimed organism, Applicant has amended Claim 1 to recite an

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"isolated" *B. subtilis*. Thus, Applicant respectfully requests that this rejection be withdrawn.

## 2) The Claims Meet the Written Description Requirement

The Examiner has rejected Claims 1-3 and 5-10 under 35 U.S.C. §112, first paragraph, as allegedly not meeting the written description requirement. Applicant must respectfully disagree.

The Examiner argues that the "specification fails to exemplify or describe either the preparation or the isolation of the subject matters of 'gram-positive' microorganisms of claims 1-3 and 5-10." (Office Action, page 5). Applicant notes that the Examiner admits that the Specification discloses the nucleic acid sequence of SEQ ID NO:1 and that the sequence is endogenous to *B. subtilis*. While Applicant must respectfully disagree with the Examiner's arguments, in order to further the prosecution of the present application and Applicant's business interests, yet without acquiescing to the Examiner's arguments, Applicant has amended Claim 1 to recite that the isolated microorganism is *B. subtilis*. Claims 2 and 3 have been cancelled and Claims 4 and 5 amended. Applicants reserve the right to pursue the original and or similar Claims in one or more subsequent applications. As the Examiner admits that the present Specification describes the metalloprotease of *B. subtilis*, Applicant respectfully submits that the Claims are allowable and requests that this rejection be withdrawn.

## 3) The Claims are Enabled

The Examiner has rejected Claims 1-3 and 5-10 stand rejected under 35 U.S.C. §112, first paragraph as allegedly not meeting the enablement requirement. Applicant must respectfully disagree.

The Examiner argues that the "specification, while being enabling for *Bacillus subtilis* cells have a mutation in, including a deletion of all or part of, a

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nucleic acid sequence encoding a metalloprotease having the amino acid sequence set forth in SEQ ID NO:2 which inactivates or eliminates the metalloprotease, does not reasonably provide enablement for finding or making other generic, gram-positive microorganisms having inactivating mutations of nucleic acid sequences encoding an amino acid sequence related to SEQ ID NO:2." (Office Action, page 7). Thus, Applicant appreciatively notes that the Examiner admits that the present Specification is enabled for mutated *B. subtilis* metalloproteases, in particular mutations in SEQ ID NO:1 or mutant SEQ ID NO:2. Although Applicant must respectfully disagree with the Examiner's arguments, in order to further Applicant's business interests and the prosecution of the present application, yet without acquiescing to the Examiner's arguments, Applicant has amended Claim 1 to recite that the mutation occurs in SEQ ID NO:2. Applicants reserve the right to pursue the original and or similar Claims in one or more subsequent applications. Applicant respectfully submits that the Claims are allowable and requests that this rejection be withdrawn.

#### 4) The Claims are Definite

The Examiner has rejected Claims 1-10 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Applicant must respectfully disagree.

The Examiner indicates that neither the independent Claim 1 or its dependent Claim 4 recite a sequence identifier. Applicant appreciates the Examiner's suggestion for amending Claim 1. Indeed in order to further Applicant's business interests and the prosecution of the present application, Applicant has amended Claim 1 to recite that the mutation occurs in SEQ ID NO:2. Applicants reserve the right to pursue the original and or similar Claims in one or more subsequent applications. Applicant respectfully submits that the Claims are allowable and requests that this rejection be withdrawn.

In addition, the Examiner has rejected Claim 5 as being indefinite for the recitation of 'nucleic acid found about 2248 kb from the point of origin' because

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this recitation erroneously indicates Applicant intends a single nucleic acid . . . .” (Office Action, page 10). In order to more clearly describe the claimed invention, Applicant has amended Claim 5 to recite that the nucleic acid encoding the metalloprotease begins at about 2248 kb from the point of origin. The Specification indicates that the point of origin for *B. subtilis* is known in the art (See, page 9). Thus, Applicant respectfully submits that this Claim is definite and requests that this rejection be withdrawn. Applicant reserves the right to pursue the original and or similar Claims in one or more subsequent applications. Applicant respectfully submits that this Claim is allowable and requests that this rejection be withdrawn.

The Examiner has also rejected Claims 6 and 7 as allegedly being indefinite in reciting ‘comprises nucleic acid encoding’, because this statement erroneously indicates that a single nucleic acid, which may be a nucleotide can encode something. Claim 10 also stands rejected as allegedly being indefinite for failure to clearly distinguish between genera and sub-genera in the recited *Markush* group. In order to more clearly describe the claimed elements, Applicant has amended Claims 6 and 7 to recite that the nucleic acid is a nucleic acid sequence that encodes either a heterologous (Claim 6) or homologous (Claim 7) protein. Claim 10 has been amended to provide a proper *Markush* group recitation. Applicants reserve the right to pursue the original and or similar Claims in one or more subsequent applications. Applicant respectfully submits that the Claims are allowable and requests that this rejection be withdrawn.

#### **5-6) The Claims are Novel**

The Examiner has rejected Claims 1-3 and 6-10 under 35 U.S.C. §102(b), as allegedly being anticipated by Ferrari *et al.* (U.S. Patent No. 5,264,366), or Sloma *et al.* (U.S. Patent Nos. 5,589,383 or 5,620,880); and Claims 1-3 and 7 have been rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Donovan *et al.*

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(U.S. Patent No. 5,759,538). Applicant must respectfully disagree. In order for a reference to anticipate the Claims, each and every element must be disclosed in the reference<sup>2</sup>. As none of these references disclose mutation or deletion of part or all of the nucleic acid encoding metalloprotease (MP) having the amino acid sequence set forth in SEQ ID NO:2, as currently claimed, these references do not anticipate the presently claimed invention. Thus, Applicants respectfully submit that the present Claims are allowable and request that this rejection be withdrawn.

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<sup>2</sup> "Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. . . . There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic & Research Fdn. v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991).


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### CONCLUSION

In light of the foregoing amendments, as well as the above remarks, Applicants believe the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-5838.

Respectfully submitted,

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